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(54) Title: METHOD FOR SELECTIVE INHIBITION OF HUMAN N-MYC GENE IN N-MYC EXPRESSING TUMORS THROUGH ANTISENSE AND ANTIGEN PEPTIDO-NUCLEIC ACIDS (PNA)

(57) Abstract: The present invention refers to sense and antisense peptido-nucleic acids (PNAs). The present invention further refers to the use of said PNAs for preparing drugs for treating genetic diseases.

WO 2004/096826 A3

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
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According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
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Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SUN LICHUN ET AL: "Antisense peptide nucleic acids conjugated to somatostatin analogs and targeted at the n-myc oncogene display enhanced cytotoxicity to human neuroblastoma IMR32 cells expressing somatostatin receptors" PEPTIDES (NEW YORK), vol. 23, no. 9, September 2002 (2002-09), pages 1557-1565, XP002322720 ISSN: 0196-9781	1-12
Y	the whole document * figure 1: DC-46-9, DC-44-79 and DC-46-3 targeting the 5'UTR terminus; JF-08-69 and JF-08-67 targeting the coding region close to the start site at position 1659-1670 * ----- -/-	2,7

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☐ Patent family members are listed in annex.

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	DOYLE DONALD F ET AL: "Inhibition of gene expression inside cells by peptide nucleic acids: Effect of mRNA target sequence, mismatched bases, and PNA length" BIOCHEMISTRY, vol. 40, no. 1, 9 January 2000 (2000-01-09), pages 53-64, XP002187945 ISSN: 0006-2960 abstract	1-6,8-12
Y	GALDERISI, U. ET AL: "Antisense inhibitory effect: a comparison between 3'-partial and full phosphorothioate antisense oligonucleotides" JOURNAL OF CELLULAR BIOCHEMISTRY (1999), 74(1), 31-37 CODEN: JCEBD5; ISSN: 0730-2312, vol. 74, 1999, pages 31-37, XP002219271 abstract page 32, left-hand column, lines 1-5 page 32, left-hand column, last paragraph	1,3-12
Y	ROSOLEN A ET AL: "ANTISENSE INHIBITION OF SINGLE COPY N-MYC EXPRESSION RESULTS IN DECREASED CELL GROWTH WITHOUT REDUCTION OF C-MYC PROTEIN IN A NEUROEPITHELIOMA CELL LINE" CANCER RESEARCH, vol. 50, no. 19, 1990, pages 6316-6322, XP001205716 ISSN: 0008-5472 abstract page 6316, right-hand column, last paragraph	1,3-12
Y	CUTRONA GIOVANNA ET AL: "Effects in live cells of a c-myc anti-gene PNA linked to a nuclear localization signal" NATURE BIOTECHNOLOGY, vol. 18, no. 3, March 2000 (2000-03), pages 300-303, XP002322722 ISSN: 1087-0156 page 300	3-5
Y	POOGA M ET AL: "CELL PENETRATING PNA CONSTRUCTS REGULATE GALANIN RECEPTOR LEVELS AND MODIFY PAIN TRANSMISSION IN VIVO" NATURE BIOTECHNOLOGY, NATURE PUB. CO, NEW YORK, NY, US, vol. 16, 1998, pages 857-861, XP000910290 ISSN: 1087-0156 abstract page 860, left-hand column, lines 28-30	3-5
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PCT/IB2004/001297

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	SIMMONS C G ET AL: "Synthesis and membrane permeability of pna-peptide conjugates" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 7, no. 23, 2 December 1997 (1997-12-02), pages 3001-3006, XP004136573 ISSN: 0960-894X page 3001, last paragraph page 3002; table 1 -----	3-5
P,X	PESSION ANDREA ET AL: "Targeted inhibition of NMYC by peptide nucleic acid in N-myc amplified human neuroblastoma cells: Cell-cycle inhibition with induction of neuronal cell differentiation and apoptosis." INTERNATIONAL JOURNAL OF ONCOLOGY, vol. 24, no. 2, February 2004 (2004-02), pages 265-272, XP009045755 ISSN: 1019-6439 the whole document -----	1-12